

**AMENDMENTS TO THE SPECIFICATION**

Please amend the following paragraphs accordingly

**Page 3, lines 8 and 16,**

an aromatic group optionally having one or more substituents, the aromatic ring having optional nitrogen, sulfur or oxygen, wherein the substituent is; hydroxy; halogen; alkyloxy; alkyl; amino; alkylamino; carboxyl; nitro; sulfonylamido, alkanesulfonyl; amido; or linear or cyclic C<sub>1</sub>-C<sub>6</sub> alkyl optionally having one or more substituents, the alkyl having an optional nitrogen, sulfur or oxygen linkage and the ~~substituents~~substituent of the alkyl being: hydroxy; halogen; alkyloxy; alkyl; amino; alkylamino; carboxyl; nitro; sulfonylamido, alkanesulfonyl; amido; an aromatic group optionally having one or more substituents selected from the group consisting of hydroxy; halogen; alkyloxy; alkyl; amino; alkylamino; carboxyl; nitro; amido; dioxoisindole; and a sulfonylamino having an aromatic group substituted with hydroxy, halogen, alkyloxy, alkyl, amino, alkylamino, carboxyl, nitro, sulfonylamido, alkanesulfonyl or amido; an aromatic group optionally having one or more substituents selected ~~form~~from the group consisting of hydroxy, halogen, alkyloxy, alkyl, amino, alkylamino, carboxyl, nitro, sulfonylamide, alkanesulfonyl and amido, the aromatic ring containing nitrogen, sulfur or oxygen; or a cyclic C<sub>3</sub>-C<sub>8</sub> alkyl optionally having one or more substituents selected from the group consisting of hydroxy, halogen, alkyloxy, alkyl, amino, alkylamino, carboxyl, nitro and amido; or

**Page 3, lines 31 and 37**

Among the compounds of formula (I) of the present invention, the preferred are:

those wherein n, R<sup>1</sup>, R<sup>2</sup> and R<sup>3</sup> have the same ~~meaning~~meanings as defined previously;

R<sup>4</sup> and R<sup>5</sup> are each independently hydrogen;

C<sub>1</sub>-C<sub>4</sub> alkyl optionally having one or more substituents selected from the group consisting of OH, NH<sub>2</sub>, NO<sub>2</sub>, and an aromatic group, the aromatic group optionally having one or more substituents selected from the group consisting of OH, C<sub>1</sub>-C<sub>4</sub> alkyloxy, NH<sub>2</sub>, NO<sub>2</sub>, methanesulfonylamino, ethanesulfonylamino, ~~toluenesulfonylamino~~toluenesulfonylamino and dioxoisindole; cyclic C<sub>3</sub>-

**Page 4, lines 3-7, 16, 25, 29, and 32**

C<sub>8</sub> alkyl optionally having one or more substituents selected from the group consisting of OH, NH<sub>2</sub> and NO<sub>2</sub>; C<sub>1</sub>-C<sub>4</sub> alkyl carrying a morpholine or ~~oxepyrrolidine~~oxopyrrolidine group which is optionally substituted with OH, NH<sub>2</sub>, NO<sub>2</sub> or -O-; C<sub>1</sub>-C<sub>4</sub> alkyl or C<sub>1</sub>-C<sub>4</sub> aminoalkyl carrying a ~~pyrrolpyrrole~~pyrrole, pyrazole, imidazole, 1,2,3-triazole, 1,2,4-triazole, isoxazole, oxazole, ~~isotiazole~~isothiazole, ~~tiazolidine~~thiazolidine, tiazole, 1,2,5-oxadiazole, 1,2,3-oxadiazole, 1,2,5-~~thiodiazole~~thiadiazole, 1,2,3-~~thiodiazole~~thiadiazole, 1,3,4-oxadiazole, 1,3,4-~~thiodiazole~~thiadiazole, pyridine, pyrimidine or triazine group which is optionally having one or more substituents selected from the group consisting of Cl, OH, NH<sub>2</sub>, NO<sub>2</sub>, C<sub>1</sub>-C<sub>4</sub> and phenyl;

cyclic C<sub>3</sub>-C<sub>8</sub> alkyl optionally having one or more substituents selected from the group consisting of OH, NH<sub>2</sub> and NO<sub>2</sub>;

an aromatic group optionally having one or more substituents selected from the group consisting of OH; NH<sub>2</sub>; hydroxyalkyl; aminoalkyl; NO<sub>2</sub>; and a C<sub>1</sub>-C<sub>4</sub> alkyl group optionally having one or more substituents selected from the group consisting of OH, NH<sub>2</sub>, NO<sub>2</sub>,

methanesulfonylamino, ethanesulfonylamino, ~~toluenesulfonylamino~~toluenesulfonylamino,  
dioxoisindole and thiophensulfonylamino; or

form, together with the  $-N-(CH_2)_n-$  moiety to which they are attached, a nitrogen  
heterocycle optionally having one or more substituents selected from the group consisting of OH,  
NH<sub>2</sub> and NO<sub>2</sub>, the heterocycle containing 1 to 3 nitrogen, sulfur or oxygen atom.

In the present invention, the compounds of formula (I) as the below are most preferred:  
those wherein n, R<sup>1</sup>, R<sup>2</sup> and R<sup>3</sup> have the same ~~meaning~~meanings as defined previously; R<sup>4</sup> and R<sup>5</sup>  
are each independently hydrogen;

C<sub>1</sub>-C<sub>4</sub> alkyl optionally having one or more substituents selected from the group consisting  
of OH, NH<sub>2</sub>, NO<sub>2</sub>, morpholine, nitropyridineamino, pyridine, ~~oxopyrrolidine~~oxopyrrolidine,  
imidazole optionally having a Cl, CH<sub>3</sub> or phenyl substituent; and phenyl optionally having one or  
more substituents selected from the group consisting of OH, NH<sub>2</sub>, methoxy, NO<sub>2</sub>,  
methanesulfonylamino, ethanesulfonylamino, ~~toluenesulfonylamino~~toluenesulfonylamino and  
dioxoisindole;

**Page 5, line 2**

NH<sub>2</sub>, NO<sub>2</sub>, methanesulfonylamino, ethanesulfonylamino,  
~~toluenesulfonylamino~~toluenesulfonylamino, dioxoisindole or thiophensulfonylamino  
substituent; or

**Page 15, lines 4-5**

wherein, *p*-TSA is *p*-toluenesulfonic acid, DMF is dimethylformamide, THF is  
tetrahydrofuran, TFA is trifluoroacetic acid, EDCI is ethyl-dimethylaminopropyl-carbodiimide

hydrochloride, DMAP is 4-dimethylaminopyridine, HOBt is N-hydroxybenzotriazole, ~~hydroxybenzotriazole~~ hydroxybenzotriazole, n, R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup>, R<sup>4</sup> and R<sup>5</sup> have the same ~~meaning~~ meanings as defined previously.

**Page 16 , lines 21 and 36**

As shown in Scheme II, the compound of formula (Ib) can be prepared by reacting 3-amino-4-methoxy benzoic acid (compound II) and an alcohol (e.g., methanol or ethanol) to obtain compound (III), adding p-toluenesulfonic acid, benzene and 4-nitrobenzonitrile ~~nitrobenzonitrile~~ nitrobenzonitrile thereto, refluxing the mixture at 80 to 200 °C, adding NaOCl thereto at room temperature and purifying by silica gel column chromatography to obtain compound (XI); dissolving the compound (XI) thus obtained in an organic solvent, adding an aqueous alkali solution (e.g., Na<sub>2</sub>CO<sub>3</sub> solution) thereto, refluxing the mixture and purifying by silica gel column chromatography to obtain compound (XII); dissolving the compound (XII) thus obtained in an alcohol, adding Pd/C thereto and refluxing the mixture to obtain compound (XIII); dissolving the compound (XIII) thus obtained in an organic solvent, adding a base (e.g., CsCO<sub>3</sub>, Na<sub>2</sub>CO<sub>3</sub>, NaHCO<sub>3</sub>, K<sub>2</sub>CO<sub>3</sub> or KHCO<sub>3</sub>), 2-chloroethylmorphine and potassium iodide thereto and stirring the mixture at room temperature to obtain compound (XIV); dissolving the compound (XIV) obtained thus in an organic solvent, adding an alkali hydrate, stirring the mixture at room temperature to obtain compound (XV); dissolving the compound (XV) thus obtained in an organic solvent, adding ~~4,5-dichloro-1-(3-aminopropyl)imidazole~~ 4,5-dichloro-1-(3-aminopropyl)imidazole and a coupling agent (e.g., EDCI, DMAP or HOBt), stirring the mixture at room temperature and purifying by silica gel

**Page 19, line 15**

Anhydrous *p*-toluene sulfonic acid (41.99 g, 220.8 mmol) was melted at 120 °C and 3-amino-4-methoxy benzoic acid methyl ester (20 g, 110.38 mmol) obtained in step 1 and benzonitrile (22.77 g, 220.8 mmol) were added thereto and stirred at 180 °C for 5 hours. The resulting solution was cooled to room temperature and the reaction was stopped by adding NaHCO<sub>3</sub> thereto. The resulting mixture was extracted with ethyl acetate, the extract was dried over MgSO<sub>4</sub> and concentrated under a reduced pressure. The concentrate was dissolved in 50% methanol and 5% NaOCl (56 Mℓ, 37.65 mmol) was added dropwise thereto. After 5 min, the resulting mixture was extracted with ethyl acetate, the extract was dried over MgSO<sub>4</sub> and concentrated under a reduced pressure. The resulting residue was purified by silica gel column ~~chromatography~~ chromatography (eluent – MeOH/CDCl<sub>3</sub> = 5 : 95, Merck, Silicagel 60) to obtain the title compound (31 g, 25.10 mmol) in a yield of 88%.

**Page 21, line 37**

Anhydrous *p*-toluene sulfonic acid (41.99 g, 220.76 mmol) was melted at 120 °C and 3-amino-4-methoxy benzoic acid methyl ester (20 g, 110.38 mmol) obtained in step 1 of Preparation Example 1 and 4-chlorobenzonitrile (22.78 g, 165.57 mol) were added thereto and stirred at 160 °C for 8 hours. The resulting solution was cooled to room temperature and the reaction was stopped by adding 1M NaHCO<sub>3</sub> thereto. The resulting mixture was extracted with ethyl acetate, the extract was dried over MgSO<sub>4</sub> and concentrated under a reduced pressure. The concentrate was dissolved in 500 ml of 50% methanol and 5% NaOCl (197 Mℓ, 132.46 mmol) was added dropwise thereto. After 5 min, the resulting mixture was extracted with ethyl acetate,

the extract was dried over  $\text{MgSO}_4$  and concentrated under a reduced pressure. The resulting residue was purified by silica gel column ~~chromatography~~ chromatography (eluent –  $\text{MeOH}$  :  $\text{CDCl}_3$  = 5 : 95,